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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/117,218	01/11/1999	SUSANNE M. BROWN	117-261	3436

7590 06/23/2004

Klarquist Sparkman Campbell Leigh & Whinston, LLP
One World Trade Center
Suite 1600
Portland, OR 97204

EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/117,218	BROWN ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed on 4/19/04 has been entered.

Amended claims 33, 37-40 are pending in the present application and they are examined on the merits herein.

Response to Amendment

The Declaration filed on 12/15/2000 under 37 CFR 1.131 has been considered but is ineffective to overcome the Randazzo reference (Virology 211:94-101, 1995).

The Randazzo reference is a statutory bar under 35 U.S.C. 102(b) and thus cannot be overcome by an affidavit or declaration under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended claims 33 and 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roizman et al. (U.S. Patent No. 6,340,673; Cited previously) in view of Randazzo et al. (Virology 211:94-101, 1995; IDS). **This is a new ground of rejection.**

The claims are drawn to a method of treating a non-neuronal cancer which does not occur in the central nervous system, and comprises a non-neuronal tumour cell, in a mammal, said method comprising the step of injecting a mammal intratumorally with an effective amount of a mutant herpes simplex virus HSV 1716, and wherein said mutant virus infects, replicates and lyses said non-neuronal tumor cell in said mammal, thereby treating the non-neuronal cancer.

Roizman et al. teach using an HSV-1 virus with a specific mutation in the γ34.5 gene to treat cancer and tumorogenic diseases both in the CNS and in all other parts of the body in a mammal including human, not necessarily limited to tumors of the CNS (see col. 5, lines 63-66; col. 9, lines 50-61; and the claims). Roizman et al. further teach direct injection of the virus into the tumor or intratumorally, and that **an exemplified HSV-1 virus** with a specific mutation in the γ34.5 gene is the recombinant virus R3617 or R3616 lacking 1kb of DNA in each copy of the γ34.5 gene (see Table 1 of col. 17; Fig. 2).

Roizman et al. do not specifically teach a method for treating a non-neuronal cancer in a mammal using the mutant herpes simplex virus strain 1716.

However, at the effective filing date of the present application, Randazzo et al. already teach that the neuroattenuated HSV-1716 mutant that has a 759-bp deletion in γ34.5 is capable of lysing various murine melanoma cells *in vitro* (Table 1; page 99, left-handed column, first paragraph), and in a clinically relevant, reproducible metastatic tumor mouse model stereotactic injection of the HSV-1716 into brain tumors of melanoma cells resulted in a statistically significant increase in the time to development of neurological symptoms and in complete tumor regression and the long-term survival of some treated animals (see abstract and Fig. 2). Randazzo et al. further teach replication of this virus is restricted to tumor cells and does not occur in the surrounding brain tissue. Addtionally, Randazzo et al. state "[t]his report shows that the neuroattenuated HSV-1 mutant 1716 is a safe and effective therapeutic agent for intracranial melanoma" (page 95, left-handed column, bottom of fourth paragraph).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time of invention was made to utilize the mutant herpes simplex virus strain 1716 taught by Randazzo et al. to treat any tumor, including non-neuronal tumors, occurring in the CNS and/or in all other parts of the body in a mammal as taught by Roizman et al. in light of the teachings of Randazzo et al. above.

An ordinary skilled artisan would have been motivated to carry out the above modification because the HSV mutant 1716 has been demonstrated to be effective of killing and lysing melanoma cells in both *in vitro* and *in vivo*. Moreover, HSV-1716 has been concluded by Randazzo et al. to be a safe and effective therapeutic agent.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Roizman et al. and Randazzo et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 33 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roizman et al. (U.S. Patent No. 6,340,673; Cited previously) in view of Randazzo et al. (Virology 211:94-101, 1995; IDS) as applied to claims 33, 37-40 above, and further in view of Martuza et al. (U.S. 6,139,834; Cited previously). **This is a new ground of rejection.**

With respect to the embodiments of claim 40, wherein the cancer is a mesothelioma, ovarian carcinoma and bladder cancer, neither Roizman et al. nor Randazzo et al. teach or mention the specific cancers as recited in the claim.

However, at the effective filing date of the present application Martuza et al. already teach that replication-competent herpes simplex viral vectors with defective expression of the γ34.5 gene are capable of killing various human tumor cells *in vivo*, including mesothelioma, melanoma, pancreatic cancer cells, prostate carcinoma cells, breast cancer cells, lung cancer cells, colon cancer cells, lymphoma cells, hepatoma cells and epidermoid carcinoma cells (see col. 3, lines 49-67, and the claims).

Accordingly, it would have been obvious for an ordinary skilled artisan to utilize the modified method based on the combined teachings of Roizman et al. and Randazzo et al. to treat non-neuronal cancers such as mesothelioma, ovarian carcinoma and bladder cancer based on the teachings of Martuza et al. above.

An ordinary skilled artisan would have been motivated to carry out the above modification because it is apparent from the teachings of Martuza et al. that replication-competent herpes simplex viral vectors with defective expression of the γ34.5 gene (HSV-1716 is one of them) are effective for killing numerous non-neuronal cancer cells, and that HSV-1716 has been demonstrated to be a safe and effective therapeutic agent by Randazzo.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Roizman et al. and Randazzo et al. and Martuza et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusions

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (703) 872-9306.

Quang Nguyen, Ph.D.

DAVID GUZO
PRIMARY EXAMINER